Letters

December 29, 1998
Department of Health and Human Services
Public Health Service
National Institutes of Health
Bethesda, Maryland 20892

The Honorable Henry A. Waxman
House of Representatives
Washington, D.C. 20515-0529

Dear Mr. Waxman:

I am writing to respond to the questions in your December 7 letter regarding the relationship of Dr. Richard Eastman of the National Institute of Diabetes and Digestive and Kidney Diseases (NIKKD) with the pharmaceutical company, Warner-Lambert. The NIH is deeply concerned about and carefully reviewing this serious matter and will take the necessary action to eliminate any problems that we identify.

Responses to your specific questions follow:

1. Under NIH policies, an employee may not receive compensation for outside activities that relate to his/her official duties and responsibilities as an NIH employee. I understand, however, that a determination by an NIH Deputy Ethics Counselor that "the financial interest is not `so substantial as to be deemed likely to affect the integrity of the services the Government may expect´ from the employee" may result in "a waiver granting permission to participate in the official matter."

Did the NIH grant Dr. Eastman such a waiver to work with Warner-Lambert? On what factual basis was such a waiver granted, given Dr. Eastman´s supervision of the DPP trial? Was this waiver ever subject to reconsideration or revision by NIH or NIDDK?

Dr. Eastman did not request and was not granted a waiver. A waiver was not applicable because he applied for an approval to participate in an "outside activity" for compensation, the approval of which involves a determination by the deciding official that the activity does not conflict with the employee´s official duties.

Under certain circumstances, NIH policy permits employees to participate in outside activities for compensation. Prior approval of these activities is required. The NIH policy is based on the Department of Health and Human Services Supplemental Standards of Conduct for Employees, at 5 CFR Part 5501. On October 31, 1995, Dr. Eastman submitted a request for approval of an outside activity with Warner-Lambert; his request was approved by the Deputy Ethics Counselor in NIDDK on November 15, 1995.

As discussed below in the answer to question 4, Dr. Eastman did recuse himself from voting on the Steering Committee of the DPP trial. A recusal is a signed statement by an employee withdrawing from participation in an official duty activity involving an outside organization with which he or she has a relationship.

Copies of the relevant regulations and guidelines regarding outside activities and conflict of interest are enclosed for your information.

2. Please specify the decisions and other official acts in which Dr. Eastman participated relating to the inclusion of Rezulin in the DPP trial.

The NIH has asked the Inspector General (IG) of the Department of Health and Human Services to examine whether NIDDK correctly applied conflict-of-interest guidelines in approving Dr. Eastman´s outside activity request and whether any violation of law or regulation occurred. A copy of the NIH request to the IG is enclosed. We will be in a position to answer your question after the completion of the IG investigation.

3. How much compensation has Dr. Eastman received from Warner-Lambert in 1995, 1996 and 1997? Please make available all relevant financial disclosure records filed by Dr. Eastman under the Ethics in Government Act.

NIH records indicate that Dr. Eastman received the following compensation from Warner-Lambert and related companies: 1995–$20,000 (consulting); 1996–$29,120 (consulting, curriculum development, and travel); 1997–$29,335 (consulting, curriculum development, and travel). I am enclosing documents that include the financial records you request. These documents have also been provided to the Los Angeles Times in connection with a Freedom of Information Act request regarding this matter.

4. Was Dr. Eastman´s arrangement with Warner-Lambert disclosed publicly? Were participants or principal investigators in the DPP trial aware of Dr. Eastman´s compensation by Warner-Lambert? Is the NIDDK or NIH concerned about the public reaction to such disclosures?

The NIH has no record of any public announcement by Dr. Eastman concerning his arrangement with Warner-Lambert; however, NIH files contain a copy of Dr. Eastman´s February 15, 1996, memorandum to the Deputy Director for Management and Operations, NIDDK, in which Dr. Eastman stated, "I have informed the Steering Committee of the Diabetes Prevention Program that I have a potential conflict of interest with Parke-Davis [the drug unit of Warner-Lambert], with whom I have a consulting arrangement. I have officially recused myself from voting on the Steering Committee." The Steering Committee is composed of the principal investigators for the study. We anticipate that the extent of Dr. Eastman´s disclosures will be clarified by the IG´s examination.

The NIH is deeply concerned about public reaction to a possible of interest. It is of utmost importance that clinical trials conducted and supported by the NIH are credible to the public and to the medical community. The public trusts the NIH to provide science-based information on new ways to prevent, diagnose, and treat diseases, so it is critical that our studies are objectively designed and carried out. An actual or even a perceived conflict of interest can impair the public´s trust in our studies and the findings that stem from them. This is one of the reasons why the NIH has requested that the IG look into the specific case relating to Dr. Eastman and why the NIH Office of Human Resource Management is now reviewing practices across the NIH regarding conflict-of-interest requirements. I have also asked that a workshop be held at the NIH which will bring together experts to advise us about conflict-of-interest issues related to medical research, most specifically to extramural research. I expect this workshop to take place in the spring or early summer of 1999.

5. Please provide any precedents or examples of NIH officials of comparable seniority and responsibility who have had comparable financial arrangements with pharmaceutical companies.

In addition to reviewing practices across the NIH regarding conflict-of-interest guidelines, the NIH Office of Human Resources Management is reviewing information about any relationships that exist between extramural staff at the NIH and private sector companies. Our review indicates that there are no comparable arrangements. We have concluded that in four outside-activity cases, approval of paid

arrangements was questionable, although these involved employees with less seniority and responsibility than Dr. Eastman. We are examining the details of these four cases and will send you additional information within two weeks.

6. A June 11, 1996 Warner-Lambert press release quotes Dr. Eastman as characterizing the selection of Rezulin for the DPP trial as follows: "The group of investigators conducting the study ... felt it [Rezulin] had a favorable safety profile, few side effects and if corrects the underlying cause of diabetes—insulin resistance."

Did Dr. Eastman make this statement? If not, has the NIDDK or NIH corrected this statement publicly?

Dr. Eastman says that he does not remember making the statement. NIDDK has requested that Warner-Lambert not use the statement (a copy of the letter making the request is enclosed), and it has been removed from the company´s Web site.

7. A December 3, 1997 Wall Street Journal article quotes Dr. Eastman as characterizing the risk of adverse reactions to Rezulin as follows: "Doctors should be concerned, they should monitor patients, and if they do that, the risk seems to be very minimal."

Is this statement consistent with the NIDDK´s June 4, 1998 announcement that it would discontinue the Rezulin arm of the DPP trial?

Dr. Eastman´s statement, as quoted, and the announcement that the Rezulin arm of the DPP trial was being discontinued are not inconsistent when considered in context. All drugs have side effects. There is a risk-benefit ratio related to the administration of drugs, depending upon the seriousness of the side effects relative to the seriousness of the disease or to the patient´s health statues. These two statements were made regarding different uses of the drug Rezulin in people who have different risk-benefit ratios, as follows:

The 1997 statement by Dr. Eastman appeared in a Wall Street Journal article regarding the withdrawal of the drug from the European market. The drug continued to be approved for use and to be marketed in the United States. This 1997 statement pertained to use of the marketed drug to treat individuals who have overt Type 2 diabetes.
In contrast, the 1998 announcement concerned the NIDDK´s discontinuation of the use of this drug in a clinical trial in which its use was being tested in people who, although at risk for developing Type 2 diabetes, did not have overt disease. After the death of a patient in the clinical trial was deemed by a panel of outside experts to have been due to drug-induced liver failure, the NIDDK Director withdrew the drug from the study, as recommended by the expert panel. A major consideration in this decision was that, following the death of this patient, the risks of using the drug were considered to outweigh the potential benefits to study participants who did not have overt Type 2 diabetes and who were taking the drug as a possible preventive agent, not as a treatment agent.
We appreciate your interest in this matter and take seriously the need to respond completely to your inquiry. We will keep you informed of our progress.

Sincerely,

Harold Varmus, M.D.
Director